

CLAIM AMENDMENTS

1. (Original) A method of designing a physiologically active peptide capable of interacting with a target amino acid sequence, comprising:

- (a1) a step for accepting an entry of sequence data on a target amino acid sequence,
- (b1) a step for converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,
- (c1) a step for generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those in step (b1),
- (d1) a step for calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,
- (e1) a step for storing a candidate for complementary amino acid sequence, along with said complementariness parameter, in a storage,
- (f1) a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (e1), and
- (g1) a step for displaying an extracted complementary amino acid sequence as a candidate for physiologically active peptide.

2. (Original) A method of claim 1, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

3. (Currently Amended) A method of claim 1 ~~or 2~~, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α -helix and β -sheet, and indices showing the relative size of side chain volume.

4. (Currently Amended) A method of claim 1 ~~any one of claims 1-3~~, characterized in that the number of candidates for complementary amino acid sequence

extracted as physiologically active peptides is narrowed down by taking steps (b1)-(f1) for a specified number of complementary amino acid sequences extracted in steps (a1)-(f1) using one or more specified amino acid indices, in one or more repeats, using one or more other amino acid indices.

5. (Original) A method of designing a physiologically active peptide capable of interacting with a target protein, comprising:

(a1') a step for accepting an entry of sequence data on a target amino acid sequence in a target protein,

(b1') a step for converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

(c1') a step for generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those in step (b1'),

(d1') a step for calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,

(e1') a step for storing a candidate for complementary amino acid sequence, along with said complementariness parameter, in a storage,

(f1') a step for extracting a specified number of candidates for complementary amino acid sequences on the basis of information stored by step (e1'),

(g1') a step for calculating an intermolecular energy parameter with a target site of target protein, for an extracted candidate for complementary amino acid sequence,

(h1') a step for storing a candidate for complementary amino acid sequence, along with said intermolecular energy parameter, in a storage,

(i1') a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (h1'), and

(j1') a step for displaying an extracted complementary amino acid sequence as a candidate for physiologically active peptide.

6. (Original) A method of claim 5, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said

target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

7. (Currently Amended) A method of claim 5 ~~or 6~~, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α -helix and β -sheet, and indices showing the relative size of side chain volume.

8. (Currently Amended) A method of claim 5 ~~any one of claims 5-7~~, characterized in that the number of candidates for complementary amino acid sequence extracted as physiologically active peptides is narrowed down by taking steps (b1')-(f1') for a specified number of complementary amino acid sequences extracted in steps (a1')-(f1') using one or more specified amino acid indices, in one or more repeats, using one or more other amino acid indices, after which steps (g1')-(i1') are taken.

9. (Original) A program for designing a physiologically active peptide capable of interacting with a target amino acid sequence, allowing a computer to execute:

- (a1) a step for accepting an entry of sequence data on a target amino acid sequence,
- (b1) a step for converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,
- (c1) a step for generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those in step (b1),
- (d1) a step for calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,
- (e1) a step for storing a candidate for complementary amino acid sequence, along with said complementariness parameter, in a storage,
- (f1) a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (e1), and
- (g1) a step for displaying an extracted complementary amino acid sequence as a candidate for physiologically active peptide.

10. (Original) A program of claim 9, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

11. (Currently Amended) A program of claim 9 ~~or 10~~, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α -helix and β -sheet, and indices showing the relative size of side chain volume.

12. (Currently Amended) A program of claim 9 ~~any one of claims 9-11~~, characterized in that the number of candidates for complementary amino acid sequence extracted as physiologically active peptides is narrowed down by taking steps (b1)-(f1) for a specified number of complementary amino acid sequences extracted in steps (a1)-(f1) using one or more specified amino acid indices, in one or more repeats, using one or more other amino acid indices.

13. (Original) A program for designing a physiologically active peptide capable of interacting with a target protein, allowing a computer to execute:

(a1') a step for accepting an entry of sequence data on a target amino acid sequence in a target protein,

(b1') a step for converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

(c1') a step for generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those in step (b1'),

(d1') a step for calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,

(e1') a step for storing a candidate for complementary amino acid sequence, along with said complementariness parameter, in a storage,

(f1') a step for extracting a specified number of candidates for complementary amino acid sequences on the basis of information stored by step (e1'),

(g1') a step for calculating an intermolecular energy parameter with a target site of target protein, for an extracted candidate for complementary amino acid sequence,

(h1') a step for storing a candidate for complementary amino acid sequence, along with said intermolecular energy parameter, in a storage,

(i1') a step for extracting a specified number of complementary amino acid sequences on the basis of information stored by step (h1'), and

(j1') a step for displaying an extracted complementary amino acid sequence as a candidate for physiologically active peptide.

14. (Original) A program of claim 13, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

15. (Currently Amended) A program of claim 13 ~~or 14~~, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α -helix and β -sheet, and indices showing the relative size of side chain volume.

16. (Currently Amended) A program of claim 13 ~~any one of claims 13-15~~, characterized in that the number of candidates for complementary amino acid sequence extracted as physiologically active peptides is narrowed down by taking steps (b1')-(f1') for a specified number of complementary amino acid sequences extracted in steps (a1')-(f1') using one or more specified amino acid indices, in one or more repeats, using one or more other amino acid indices, after which steps (g1')-(i1') are taken.

17. (Currently Amended) A computer-readable recording medium containing a program of claim 9 ~~any one of claims 9-16~~.

18. (Original) An apparatus for designing a physiologically active peptide capable of interacting with a target amino acid sequence, provided with (A) a data entry portion, (B) a data editing portion, (C) a complementary amino acid sequence candidate generation portion, (D) a complementariness calculation portion, (E) a complementary amino

acid sequence candidate memory portion, (F) a complementary amino acid sequence search portion, and (G) a complementary amino acid sequence display portion, wherein:

said data entry portion includes (a1) a means of accepting an entry of sequence data on a target amino acid sequence,

said data editing portion includes (b1) a means of converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

said complementary amino acid sequence candidate generation portion includes (c1) a means of generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those for means (b1),

said complementariness calculation portion includes (d1) a means of calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence,

said complementary amino acid sequence candidate memory portion includes (e1) a means of storing a candidate for complementary amino acid sequence, along with said complementariness parameter,

said complementary amino acid sequence search portion includes (f1) a means of extracting a specified number of complementary amino acid sequences on the basis of information stored by means (e1), and

said complementary amino acid sequence display portion includes (g1) a means of displaying a complementary amino acid sequence extracted by means (f1) as a candidate for physiologically active peptide.

19. (Original) An apparatus of claim 18, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

20. (Currently Amended) An apparatus of claim 18 ~~or 19~~, wherein said amino acid index is one or more indices selected from among indices based on the degree of

hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α -helix and β -sheet, and indices showing the relative size of side chain volume.

21. (Original) An apparatus for designing a physiologically active peptide capable of interacting with a target protein, provided with (A) a data entry portion, (B) a data editing portion, (C) a complementary amino acid sequence candidate generation portion, (D) a complementariness calculation portion, (E) a complementary amino acid sequence candidate memory portion, (F) a complementary amino acid sequence search portion, and (G) a complementary amino acid sequence display portion, wherein:

said data entry portion includes (a1') a means of accepting an entry of sequence data on a target amino acid sequence in a target protein,

said data editing portion includes (b1') a means of converting said target amino acid sequence to one or more moving average profile waveforms in accordance with one or more specified amino acid indices,

said complementary amino acid sequence candidate generation portion includes (c1') a means of generating a candidate for an amino acid sequence complementary to target amino acid sequence, and converting it to one or more complementary moving average profile waveforms using the same one or more amino acid indices as those for means (b1'),

said complementariness calculation portion includes (k1') a means of calculating each of complementariness parameters from the same amino acid index between one or more moving average profile waveforms for said target amino acid sequence and one or more complementary moving average profile waveforms of a candidate for complementary amino acid sequence, and further calculating an intermolecular energy parameter with a target site of target protein,

said complementary amino acid sequence candidate memory portion includes (l1') a means of storing a candidate for complementary amino acid sequence, along with said complementariness parameter and said intermolecular energy parameter,

said complementary amino acid sequence search portion includes (m1') a means of extracting a specified number of complementary amino acid sequences on the basis of information stored by means (k1'), and

said complementary amino acid sequence display portion includes (n1') a means of displaying a complementary amino acid sequence extracted by said complementary amino acid sequence search portion as a candidate for physiologically active peptide.

22. (Original) An apparatus of claim 21, wherein said complementariness parameter is the correlation coefficient between a moving average profile waveform for said target amino acid sequence and a complementary moving average profile waveform of a candidate for complementary amino acid sequence.

23. (Currently Amended) An apparatus of claim 21 or 22, wherein said amino acid index is one or more indices selected from among indices based on the degree of hydrophobicity, indices based on an electric property, indices showing the likelihood of taking the α -helix and β -sheet, and indices showing the relative size of side chain volume.

24. (Currently Amended) A program of claim 13 ~~any one of claims 13-16~~, further including between step (i1') and step (j1'):

(I) a step for generating an amino acid sequence with an amino acid variation introduced to an amino acid sequence extracted in step (i1'),

(II) a step for calculating an intermolecular energy parameter between an amino acid sequence generated in step (I) and a target site of target protein, and

(III) a step for comparing an intermolecular energy parameter calculated in step (II) with an intermolecular energy parameter between an amino acid sequence extracted in step (i1') and a target site of target protein as a control, and extracting an amino acid sequence having an intermolecular energy parameter that is stabler than the intermolecular energy parameter of the control.

25. (Original) A program for designing a physiologically active peptide capable of interacting with a target protein, allowing a computer to execute:

(a2) a step for identifying the interaction region in a protein that interacts with a target site of target protein, and

(b2) a step for extracting an amino acid sequence of an optionally chosen length from said interaction region.

26. (Original) A program for designing a physiologically active peptide capable of interacting with a target protein, allowing a computer to execute:

(a2') a step for identifying the interaction region in a protein that interacts with a target site of target protein,

(b2') a step for extracting an amino acid sequence of an optionally chosen length from said interaction region,

(c2') a step for calculating an intermolecular energy parameter with a target site of target protein, for an extracted amino acid sequence,

(d2') a step for storing said amino acid sequence, along with said intermolecular energy parameter, in a storage,

(e2') a step for extracting a specified number of amino acid sequences on the basis of information stored by step (d2'), and

(f2') a step for displaying an extracted amino acid sequence as a candidate for physiologically active peptide.

27. (Original) A program of claim 26, further including between step (e2') and step (f2'):

(I) a step for generating an amino acid sequence with an amino acid variation introduced to an amino acid sequence extracted in step (e2'),

(II) a step for calculating an intermolecular energy parameter between an amino acid sequence generated in step (I) and a target site of target protein, and

(III) a step for comparing an intermolecular energy parameter calculated in step (II) with an intermolecular energy parameter between an amino acid sequence extracted in step (e2') and a target site of target protein as a control, and extracting an amino acid sequence having an intermolecular energy parameter that is stabler than the intermolecular energy parameter of the control.

28. (Original) A program for designing a physiologically active peptide capable of interacting with a target protein, allowing a computer to execute:

(a3) a step for exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,

(b3) a step for calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,

(c3) a step for generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated in step (b3),

(d3) a step for calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,

(e3) a step for conducting a correlation analysis between an intermolecular energy parameter calculated in step (b3) and said score to obtain a regression equation,

(f3) a step for converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,

(g3) a step for calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter, and

(h3) a step for extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value.

29. (Original) A program for designing a physiologically active peptide capable of interacting with a target protein, allowing a computer to execute:

(a3') a step for exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,

(b3') a step for calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,

(c3') a step for generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated in step (b3'),

(d3') a step for calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,

(e3') a step for conducting a correlation analysis between an intermolecular energy parameter calculated in step (b3') and said score to obtain a regression equation,

(f3') a step for converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,

(g3') a step for calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter,

(h3') a step for extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value,

(i3') a step for calculating an intermolecular energy parameter with a target site of target protein, for an extracted amino acid sequence,

(j3') a step for storing said amino acid sequence, along with said intermolecular energy parameter, in a storage,

(k3') a step for extracting a specified number of amino acid sequences on the basis of information stored by step (j3'), and

(l3') a step for displaying an amino acid sequence extracted in step (k3') as a candidate for physiologically active peptide.

30. (Original) A program of claim 29, further including between step (k3') and step (l3'):

(I) a step for generating an amino acid sequence with an amino acid variation introduced to an amino acid sequence extracted in step (k3'),

(II) a step for calculating an intermolecular energy parameter between an amino acid sequence generated in step (I) and a target site of target protein, and

(III) a step for comparing an intermolecular energy parameter calculated in step (II) with an intermolecular energy parameter between an amino acid sequence extracted in step (k3') and a target site of target protein as a control, and extracting an amino acid sequence having an intermolecular energy parameter that is stabler than the intermolecular energy parameter of the control.

31. (Original) An apparatus for designing a physiologically active peptide capable of interacting with a target protein, provided with (A2) an interaction region identification portion, (B2) a first amino acid sequence search portion, (C2) an intermolecular energy calculation portion, (D2) an amino acid sequence memory portion, (E2) a second amino acid sequence search portion, and (F2) an amino acid sequence display portion, wherein:

said interaction region identification portion includes (a2') a means of identifying the interaction region in a protein molecule that interacts with a target site of target protein,

said first amino acid sequence search portion includes (b2') a means of extracting an amino acid sequence of an optionally chosen length from said interaction region,

said intermolecular energy calculation portion includes (c2') a means of calculating an intermolecular energy parameter with a target site of target protein, for an extracted amino acid sequence,

said amino acid sequence memory portion includes (d2') a means of storing said amino acid sequence, along with said intermolecular energy parameter, in a storage,

said second amino acid sequence search portion includes (e2') a means of extracting a specified number of amino acid sequences on the basis of information stored by means (d2'), and

said amino acid sequence display portion includes (f2') a means of displaying an extracted amino acid sequence as a candidate for physiologically active peptide.

32. (Original) An apparatus for designing a physiologically active peptide capable of interacting with a target protein, provided with (A3) a first amino acid sequence search portion, (B3) a first intermolecular energy calculation portion, (C3) a score matrix generation portion, (D3) a score calculation portion, (E3) a regression equation generation portion, (F3) a matrix conversion portion, (G3) an amino acid position-dependent energy calculation portion, (H3) a second amino acid sequence search portion, (I3) a second intermolecular energy calculation portion, (J3) an amino acid sequence memory portion, (K3) a third amino acid sequence search portion, and (L3) an amino acid sequence display portion, wherein:

said first amino acid sequence search portion includes (a3') a means of exhaustively generating amino acid sequences of constant length, and randomly selecting amino acid sequences from among them for extraction as a library for analysis,

said first intermolecular energy calculation portion includes (b3') a means of calculating an intermolecular energy parameter for each of the amino acid sequences extracted as a library for analysis,

said score matrix generation portion includes (c3') a means of generating a score matrix based on amino acid prevalence using an intermolecular energy parameter calculated by means (b3'),

said score calculation portion includes (d3') a means of calculating a score based on amino acid prevalence using a score matrix based on amino acid prevalence,

said regression equation generation portion includes (e3') a means of conducting a correlation analysis between an intermolecular energy parameter calculated by means (b3') and said score to obtain a regression equation,

said matrix conversion portion includes (f3') a means of converting a score matrix based on amino acid prevalence to a matrix based on an amino acid position-dependent intermolecular energy parameter using said regression equation,

said amino acid position-dependent energy calculation portion includes (g3') a means of calculating an amino acid position-dependent intermolecular energy parameter value from a matrix based on an amino acid position-dependent intermolecular energy parameter,

said second amino acid sequence search portion includes (h3') a means of extracting an amino acid sequence not higher than a specified amino acid position-dependent intermolecular energy parameter value,

said second intermolecular energy calculation portion includes (i3') a means of calculating an intermolecular energy parameter with a target site of target protein, for an extracted amino acid sequence,

said amino acid sequence memory portion includes (j3') a means of storing said amino acid sequence, along with said intermolecular energy parameter, in a storage,

said third amino acid sequence search portion includes (k3') a means of extracting a specified number of amino acid sequences on the basis of information stored by step (j3'), and

said amino acid sequence display portion includes (l3') a means of displaying an amino acid sequence extracted in step (k3') as a candidate for physiologically active peptide.

33. (New) A computer-readable recording medium containing a program of claim 13.